

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
2 September 2004 (02.09.2004)

PCT

(10) International Publication Number
WO 2004/074513 A1

- (51) International Patent Classification⁷: **C12Q 1/68** (74) Agent: **GRUBB, Philip**; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).
- (21) International Application Number: **PCT/EP2004/001692** (81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date: 20 February 2004 (20.02.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/449,018 21 February 2003 (21.02.2003) US
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- (84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: **METHODS FOR THE PREDICTION OF SUICIDALITY DURING TREATMENT**

(57) Abstract: This invention provides methods to predict the likelihood of suicidal or self-destructive behavior in a patient during treatment. The method employs the detection of a polymorphism in the SLC6A3 gene at Exon 9 A59G or a surrogate marker, by various methods. Also provided are methods of treatment based on the presence or absence of this polymorphism or surrogate marker. Also provided are kits to use in the methods of the invention.

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INTERNATIONAL SEARCH REPORT

 Int'l Patent Application No
 PCT/EP2004/001692

 A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, BIOSIS, MEDLINE, EMBASE, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GREENWOOD T A ET AL: "EVIDENCE FOR LINKAGE DISEQUILIBRIUM BETWEEN THE DOPAMINE TRANSPORTER AND BIPOLAR DISORDER" AMERICAN JOURNAL OF MEDICAL GENETICS, NEW YORK, NY, US, vol. 105, no. 2, 8 March 2001 (2001-03-08), pages 145-151, XP009002741	1, 37, 39-41
Y	page 146, column 1, line 11-18 page 146, column 2, line 2-5 page 146, column 2, line 18-21 page 148, column 2, line 19-30 abstract table 1 table 2 table 3 --- -/-	2, 4, 5, 12-36, 38

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

14 May 2004

Date of mailing of the international search report

09/06/2004

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	MELTZER HERBERT Y ET AL: "Clozapine treatment for suicidality in schizophrenia: International suicide prevention trial (InterSePT)." ARCHIVES OF GENERAL PSYCHIATRY, vol. 60, no. 1, January 2003 (2003-01), pages 82-91, XP009030247 ISSN: 0003-990X (ISSN print) page 88, column 2, line 38-42 abstract table 6	2,4,5
Y	BADRI F ET AL: "Dopamine and serotonin system genes may predict clinical response to clozapine" AMERICAN JOURNAL OF HUMAN GENETICS, vol. 59, no. 4 SUPPL., 1996, page A247 XP009030429 46th Annual Meeting of the American Society of Human Genetics; San Francisco, California, USA; October 29-November 2, 1996 ISSN: 0002-9297 abstract	2,4,5
Y	BASILE VINCENZO S ET AL: "Pharmacogenomics in schizophrenia: The quest for individualized therapy" HUMAN MOLECULAR GENETICS, vol. 11, no. 20, 2002, pages 2517-2530, XP002279127 ISSN: 0964-6906 page 2526, column 2, line 22-24 abstract	12-36, 38
A	GONZALES MATTHEW J ET AL: "Synonymous-non-synonymous mutation rates between sequences containing ambiguous nucleotides (Syn-SCAN)" BIOINFORMATICS (OXFORD), vol. 18, no. 6, June 2002 (2002-06), pages 886-887, XP002279126 ISSN: 1367-4803 page 886, column 1, line 28,29	6-11
A	DONOVAN DAVID M ET AL: "Human and mouse dopamine transporter genes: Conservation of 5'-flanking sequence elements and gene structures" MOLECULAR BRAIN RESEARCH, vol. 30, no. 2, 1995, pages 327-335, XP002279456 ISSN: 0169-328X figure 2	1,2,4-19

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/001692

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 39
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Diagnostic method practised on the human or animal body
2. ☒ Claims Nos.: 3
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 3

The subject-matter of claim 3 relates to a method of predicting the likelihood of suicidal or self destructive behavior or a Type 1 event occurring during treatment of a patient comprising the determination whether or not a surrogate marker for the SLC6A3 exon 9 A59G polymorphism is present in a patient.

However, the application is silent as to any technical feature of the said "surrogate marker" or any examples of such markers and the term alone is not sufficient for the skilled person to understand the actual scope of the claim.

Claim 3 is, therefore, so unclear (Art. 6 PCT) that no meaningful search of its subject-matter could be carried out.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.